REMARKS

The Invention.

The present invention provides methods for improved protein production from a cell culture using culture components and conditions that dramatically increase the amount of protein produced. The improved methods can be used for the production of proteins encoded by naturally occurring cellulase genes as well as from various heterologous constructs.

The claimed invention requires that the method use an inducing feed composition as a component of the feed stream (either batch or continuous) to induce cellulase production or proteins under the control of certain promoters. Lactose is the usual carbon source used in the production of cellulases. Sophorose is the most potent inducer of cellulase expression. Glucose, the main component of the inducing feed composition, although less expensive than both lactose and sophorose, represses cellulase expression. The inventors have found that the production costs of proteins regulated by certain promoters can be reduced by using an *in situ* cellulase-treated concentrated glucose solution described by the present invention.

Status of the Application.

Claims 15-32 are pending in the application. Claims 1-14 and 33 have been cancelled as drawn to a non-elected invention without prejudice and Applicants reserved the right to file further continuation applications on any subject matter disclosed in the instant application or on the subject matter of any previously or presently cancelled claim. Claim 15 have been amended to be in independent format. Claims 34 and 35 are new and find support throughout the specification as filed. Applicants assert new matter has not been introduced by the amendment.

Election/Restriction.

Claims 1-14 and 33 have been withdrawn by the Examiner as being drawn to a non-elected invention. Applicants hereby cancel Claims 1-14 and 33 without prejudice. Applicants reserve the right to pursue the originally filed, similar and/or broader Claims in the future.

35 U.S.C. §112, second paragraph.

Claims 15-32 stand rejected under 35 USC §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, Claims 15-32 are dependent on non-elected claims.

Claim 15 has been re-written in independent format. Claim 15 and the claims dependent therefrom are now believed to be definite. Withdrawal of the rejection is respectfully requested.

35 U.S.C. §102.

It is well-settled law that to anticipate a claim the prior art reference must contain each and every element within the four corners of the document. Thus, Applicants submit that there can be no anticipation unless all of the same elements of the invention are found within the four corners of a single reference. *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767-68 (Fed. Cir. 1987). A reference that merely contains substantially the same elements or only broadly teaches the invention is insufficient to establish anticipation. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 756 F.2d 1556, 1560, 225 USPQ 253, 256 (Fed. Cir. 1985). The Federal Circuit has stated that "anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabling to one of skill in the art." *Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc.*, 246 F.3d 1368, 1379, 58 USPQ2d 1508, 1516 (Fed. Cir. 2001). Thus, "even if the claimed invention is disclosed in a printed publication, that disclosure will not suffice as prior art if it was not enabling." *In re Donohue*, 766 F.2d 531, 533, 226 USPQ 619, 621 (Fed. Cir. 1985), *citing In re Borst*, 345 F.2d 851, 855, 45 USPQ 554, 557 (CCPA 1965), *cert. denied*, 382 U.S. 973, 148 USPQ 771 (1966).

35 U.S.C. §102(b).

Claims 15-28 and 31-32 stand rejected under 35 USC §102(b) as being anticipated by Mitchinson *et al.* (US Pat. No. 6,268,328). Specifically, the Examiner asserts that Mitchinson *et al.* teaches all the limitations of the claimed invention.

Applicants submit that the Mitchinson *et al.* is not appropriate prior art as it fails to teach each and every element of the claimed invention. Furthermore, it is not enabling.

Applicants have amended claim 15 to incorporate the limitations of claim 1. As noted above, the claimed invention uses an inducing feed composition as a component of the feed stream to induce cellulase production.

The Examiner has urged that "since the claim does not recite the specific components of the 'inducing feed composition' it is deemed...that it is equivalent to the culture media disclosed in the cited reference." Applicants believe this is an untenable statement. First, media for the cultivation of microorganisms contain the substances necessary to support the growth of microorganisms including a carbon source for incorporation into biomass. Second, fermentation conditions can be optimized to provide for the maximum increase in biomass utilizing glucose. However, as noted above, glucose is a known repressor of cellulase expression. If the Examiner is asserting that the media used in Mitchinson *et al.* contains between about 5% and 75% glucose and induces cellulase expression, then Applicants assert that Mitchinson *et al.* fails to provide any details on the growth medium. Although Mitchinson *et al.* states that "Any growth medium can be used in the present invention that is suitable to grow the desired transformants" and refers to a "liquid media" it thoroughly lacks any guidance on the components of such a medium.

Mitchinson *et al.* is not only silent on the addition of an inducing feed composition but also on the critical aspect of how they were able to induce protein production in the presence of glucose. Thus, Mitchinson *et al.* fails to provide an enabling disclosure and fails as prior art as noted above. See *Bristol-Myers Squibb Co.* and *In re Donohue.*

Finally, Example 2 on pages 23 and 24 of the instant specification shows that it is not the medium but the inducing feed composition that induces protein production when the cells are grown under otherwise identical conditions. Therefore, one skilled in the art would not have found the instant invention in the cited art and (all of) the cited references fail to anticipate the claimed invention.

Withdrawal of the rejection is respectfully requested.

35 U.S.C. §102(e).

Claims 15-28 and 31-32

Claims 15-28 and 31-32 stand rejected under 35 USC §102(e) as being anticipated by Fowler et al. (US Pat. No. 6,407,046). In addition, Claims 15-18 and 23-29 stand rejected under 35 USC §102(e) as being anticipated by Lehmbeck (US Pat. No. 6,352,841). Specifically, the Examiner asserts that Fowler *et al.* and Lehmbeck each teach all the limitations of the claimed invention.

For the reasons given above related to the Mitchinson *et al.* reference, Applicants assert that the Fowler *et al.* and the Lehman references each fail to anticipate the claimed invention. The disclosure of Fowler *et al.* is virtually identical to the Mitchinson *et al.* disclosure. Lehmbeck, at best, states that "A mixture of 20% maltose liquor and 8% urea was added continuously; phosphoric acid was added as necessary to maintain a pH of 7" but states nothing about using a concentrated glucose solution. Therefore, neither one provides any reason to believe that they disclose, let alone enable, an inducing feed composition.

Withdrawal of the rejections is respectfully requested.

CONCLUSION

In light of the above amendments, as well as the remarks, the Applicants believe the pending claims are in condition for allowance and issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (650) 846-7615.

Respectfully submitted,

Dated: Aug 31, 2005

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